IV. Filicales.

(*a*) Simplices.

Marattiaceæ.
Osmundaceæ.
Schizaeaceæ.
Gleicheniaceæ.
Matonineæ.

(*b*) Gradatæ.

Loxsomaceæ.
Hymenophyllaceæ.
Cyatheaceæ.
Dicksonieæ.
Dennstaedtiinæ.
Hydropterideæ (?).

(*c*) Mixtæ.

Davallieæ.
Lindsayeæ.
Pterideæ, and other Polypodiaceæ.

V. Equisetales.

Equisetaceæ.
Calamarieæ.

"On the Negative Variation in the Nerves of Warm-blooded Animals." By N. H. Alcock, M.D. Communicated by A. D. Waller, M.D., F.R.S. Received January 17,—Read February 12, 1903.

(From the Physiological Laboratory, University of London, S.W.)

Introduction.

The negative variation in the nerves of warm-blooded animals has already been the subject of several researches.* While the nerves are still in connection with the tissues it has been the experience of most observers that there is no difficulty in examining the negative variation,

* Valentin, 'Pflüger's Archiv,' vol. 1, p. 423; Fredericq, 'Du Bois Archiv,' 1880, p. 70; Hermann, 'Physiologie,' vol. 2, p. 120; Gotch and Horsley, 'Phil. Trans.,' "Croonian Lecture," 1891, p. 267; Macdonald and W. Reid, 'J. Physiol.,' vol. 23, p. 100; Waller, 'Animal Electricity,' London, 1897; Boruttau, (*a*) 'Centralbl. f. Physiologie,' vol. 12, p. 317, 1898, (*b*) 'Pflüger's Archiv,' vol. 84, p. 309, 1901.

but with regard to isolated nerves contradictory statements have been made, and it was to ascertain if possible the reason of this discrepancy that the present research was undertaken.

Methods.

The following method was employed in all the experiments here quoted. The animal was killed by decapitation, and the body left undisturbed for 30—45 minutes. The nerves were then dissected out, placed in a 1·05 per cent. NaCl solution at about 30° C., and kept at this temperature for about half-an-hour or more. They were then allowed to cool to room temperature (17—19° C.), and it was found that, as a rule, the negative variation of nerves so treated was of the order of 1 millivolt (*vide infra*). This, of course, is not an absolute value of the true P.D. between active and inactive parts of nerve, but only a fraction of it, depending upon the amount of internal derivation in a nerve trunk by indifferent conducting tissue.

From about 2 to 6 hours *post-mortem* this value remains at a fairly constant amount, for instance, in Experiment B^d, the sciatic of the rabbit was used 5 h. 30 m. *post-mortem*, and gave a negative variation of 0·00083 volt; in Experiment A^k, 2 h. 40 m. *post-mortem* the value was 0·00076 volt, and these are typical instances. The table on p. 277 gives the result of twenty-two experiments, in which the values were taken for heat determination, which illustrates this.

Certain points may be here noted. The practice of placing nerves in salt solution for some time before use has been employed by Waller,* Gotch,† and Boycott,‡ in the case of the frog.§

The effect of changes in the composition of the salt solution is the subject of another research which I hope to publish at a future time; however, I may here state that small differences in the concentration of the solution—*e.g.*, ±0·1 per cent. NaCl—make no apparent difference in the condition of the nerve, and the same is true in the main of *small* differences in the reaction, and of small differences of temperature.

Waller‖ has pointed out that the presence of lactose in the solution is of advantage, and taking a greater value of the negative variation for a sign of greater irritability, the same appears to be true in mammalian nerve for maltose and glucose, though I make the statement at present with some reserve.

For instance:—Experiments B^{tc} and B^{td}.

* Waller, 'Brain,' vol. 73, 1896, p. 43, *et seq.*

† Gotch, 'J. Physiol.,' vol. 28, p. 32.

‡ Boycott, *loc. cit.*

§ See also Gotch and Horsley, *loc. cit.* Macdonald and Reid, *loc. cit.*

‖ Waller, *loc. cit.* (Lectures), p. 73.

Young Rabbit.

Nerves kept for 3^h circa *post-mortem*.

Experiment No.	Temp. of nerve.	Volt. of neg. var. at excit. 100.	Volt. of neg. var. at excit. 30.	Notes.
B^{tc}	30° C.	0·00033	0·00023	1·05 p. c. NaCl + 0·5 p. c. maltose. R. sciatic.
B^{td}	30° C.	0·00023	0·00016	1·05 p. c. NaCl only. L. sciatic.

The two nerves of opposite sides are here compared, and the comparison is in favour of the R. sciatic which had been treated with maltose. No account is here possible of the precautions used to exclude fallacy, but many further experiments support the one quoted, and it is at least very probable that the maltose is the active variant.

The method employed for determining the negative variation and the action of anæsthetics was in all cases that of Waller. An additional larger box was used, with a false bottom of wood, on which the nerve chamber rested. Below this was a layer of water, so that the nerve was kept in an atmosphere nearly saturated with water vapour at whatever temperature was desired.

The standard "Berne" coil, worked with two Leclanché cells, was used to give the excitation, which always consisted of tetanising shocks for a period of 13 seconds, repeated once a minute. The number of units used was 500, when not otherwise stated. The usual precautions against current escape and electrotonus were carefully observed; this was found to be particularly necessary in the case of bird's nerve.

Half-grown rabbits were found very suitable animals to use, as the small amount of connective tissues permitted the nerves to be dissected out with a minimal amount of injury. Experiments were also made with cats, kittens, guinea-pigs, hedgehogs, pigeons, and frogs. The technique is considerably easier in the case of young animals; adults, however, answer well if care be taken. In the latter, and especially in the nerves of birds, it is advisable to work at rather higher temperatures than those given above.

Voltage and Strength of Excitation.

The voltage of the negative variation varies with the animal, the nerve employed, the temperature and condition of the nerve, and, within certain limits, with the strength of excitation.

The question of temperature will be considered later. Assuming for the present purpose that the conditions of experiment were equally favourable throughout, and taking the sciatic nerve as a standard, different animals gave the following values :—

	Millivolts.		
	Maximum observed.	Mean.	
Rabbit	1·1	0·69	Mean of 11 experiments.
Kitten	0·66	0·50	,, 5 ,,
Pigeon	1·05	0·42	,, 5 ,,
Guinea-pig	1·2	0·89	,, 2 ,,

All these are very much less than the frog, which gives 2 millivolts or more.

Different nerves in the same animal often show individual inequalities, but as a rule the larger nerves give a smaller negative variation than those of less diameter. The sciatic gives commonly the least, but is the most resistant to adverse influences. The median and ulnar nerves are more delicate, but give larger variation under favourable circumstances, *e.g.*, the median nerves of the pigeon gave a mean value of 0·54 millivolt (five experiments) as against 0·42 for the sciatic. The greatest value I have yet measured was in a branch of the anterior crural of the rabbit, which on the right side gave 2·5 millivolts and on the left 2·3.

Boruttau* found the vagus in the rabbit to give a larger negative variation than the sciatic, and obtained only very small responses from the nerves of hens, ducks, or pigeons.

The larger number of fibres not in contact with the longitudinal electrode would appear to act as a deriving circuit of less resistance in the larger nerves, and so less current passes through the galvanometer, and the greater amount of connective tissue in the sciatic would have the same effect. It is possible that there are other causes in addition to these; there is at present no evidence for or against such a possibility.

Similar reasons probably also explain why a stronger stimulus is necessary for the warm-blooded nerves than for the frog. The difference is, however, not very great. The minimal effective excitation I have so far observed is 6 units of the "Berne" coil, 500 units is commonly a maximum, 1000 nearly always so. The smaller electrical

* Boruttau (*a*), *loc. cit.*

resistance of the mammalian nerve between the exciting electrodes must be borne in mind in these comparisons.

Gotch* has recently stated that in determining the sub-maximal response of frog's nerve, the excitation of a smaller number of fibres is a far more potent cause than the varying response of each fibre, and it seems very probable that the higher threshold and wide range of excitation in mammalian nerves is due to the failure of the exciting current to reach the more distant fibres, protected as they are by intervening fibres and connective tissue, and not to any essential difference in the nerves.

The negative variation commonly persists without great alteration under ordinary conditions for at least 4—8 hours *post-mortem*. The longest time I have seen was in Experiment C^{df} (internal popliteal of the hedgehog, 28 hours *post-mortem*); the right and left median nerves the kitten in Experiments C^{eg} and C^{ef} gave a small and rapidly diminishing response 19 hours *post-mortem*.

The earlier observers (Valentin, Fredericq, Hermann) have stated that they have found the negative variation to persist for days, and to last longer than in frog's nerve. I am unable to confirm this; even in the hedgehog the nerves are much more short-lived than in the frog under similar conditions, and the phenomena referred to were probably of a different nature to those examined here, viz., electrotonic spread or ordinary diffusion.

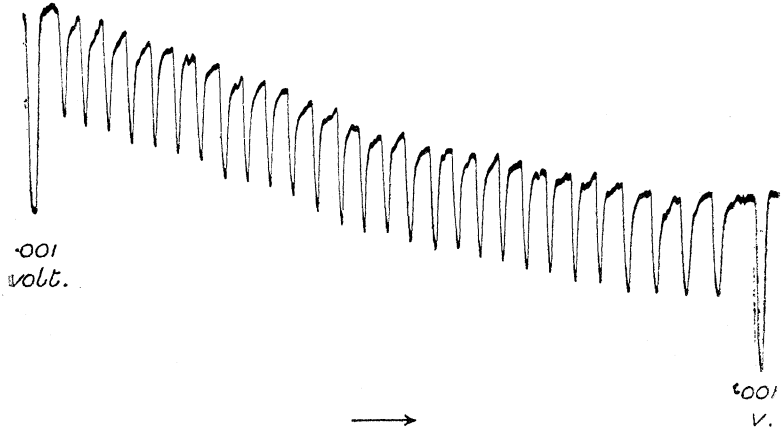

FIG. 1.—Rabbit. R. ext. popliteal. Normal series of negative variations. Exp. B^a. Reads from left to right.

* Gotch, 'J. Physiol.,' vol. 28, p. 40.

Action of Anæsthetics.

The following is the summary of the observations made on this subject :—

Chloroform.

Experiment and plate No.	Negat. var. before.	During $CHCl_3$.	After.	Notes.
	$\frac{1}{1000}$ volt.			
204	0·48	0·42 to 0 3 min.	0 to 0·42	Kitten. Sciatic. Temp. of nerve chamber, 32°. Complete abolition and recovery.
207	0·38	0·38 to 0 5 min.	0 to 0·22	Kitten. Sciatic. Temp. = 30° C. After $CHCl_3$ a positive variation appeared, changing again to a negative. Fair recovery.
A° 408	0·95	0·70 to 0·40 3 min.	0·21 to 0·13	Rabbit. L. sciatic. 6 h. *post-mortem*. Temp. = 20°. Gradual progressive diminution and no recovery. *FIG.* 3.
C^{cc} 424	0·46	0·46 to 0·15 4 min.	0·18 to 0·36	Kitten. L. median. Temp. = 32°. $CHCl_3$ dilute at first, stronger after first minute.
B^{i} 417	0·47	0·6 to 0·1 5 min.	0·21 to 0·40	Pigeon. R. median. 3 h. *post-mortem*. Temp. 37°. Recovery.

Ether.

		During ether.		
201	0·40	0·25 to 0 3 min.	0 to 0·28	Kitten. R. sciatic. Temp. 34°. 37 m. *post-mortem*. Imperfect recovery.
203	0·66	0·25 to 0 3 min.	0 to 0·46	Kitten. L. sciatic. 4 h. *post-mortem*. Temp. = 28°. Recovery.
B^{b} 413	0·54	0·22 to 0 3 min.	0 to 0·54	Rabbit. Ext. popliteal. 2 h. 30 m. *post-mortem*. Temp. = 30°. Recovery. *FIG.* 2.
B^{h} 416	0·83	— to 0 2 min.	0 to 0·51	Pigeon. 2 h. 30 m. *post-mortem*. Temp. = 39° C. L. sciatic. Recovery.

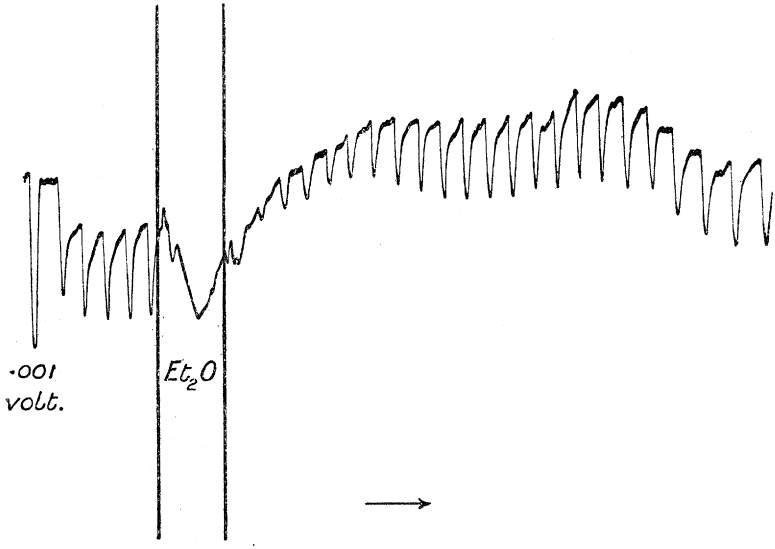

Fig. 2.—Rabbit. Same nerve as fig. 1. Ether vapour. Exp. B^b.

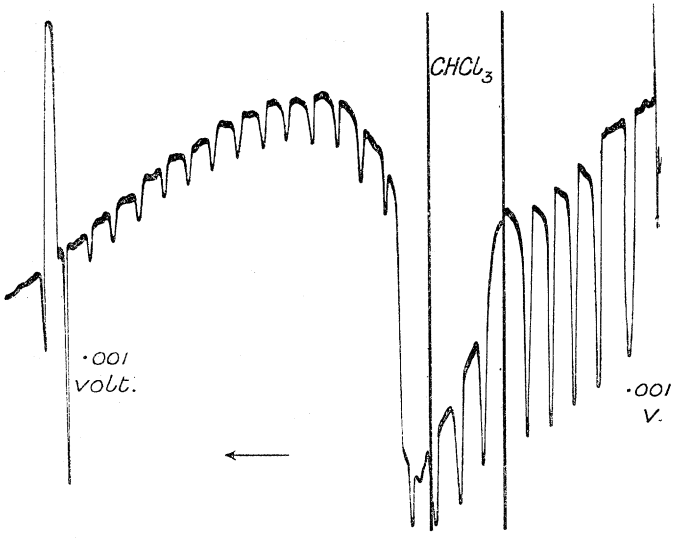

Fig. 3.—Rabbit. L. sciatic. Chloroform vapour. Reads from right to left. Exp. A°.

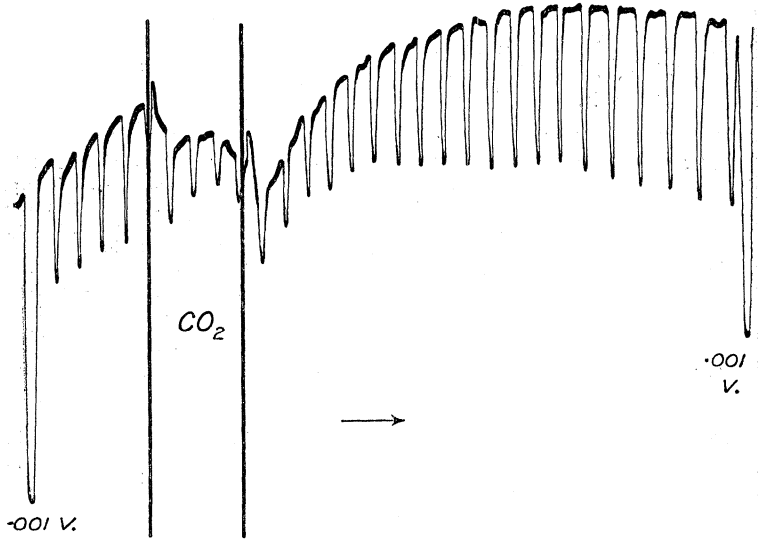

FIG. 4.—Rabbit. R. sciatic. CO_2. Exp. A[1].

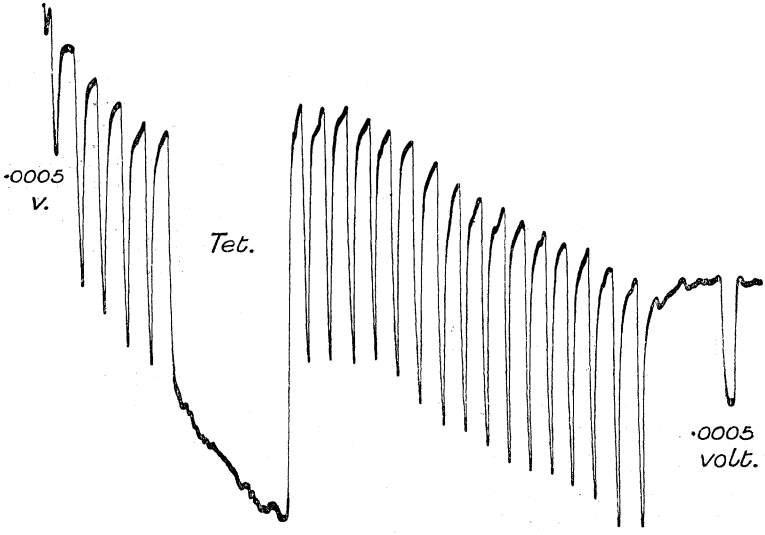

FIG. 5.—Rabbit. R. sciatic. Tetanisation for 5 m. Exp. A[1].

CO_2.

Experiment and plate No.	Neg. var. before in 0·001 volt.	Neg. var. during CO_2.	Neg. var. after.	Notes.
202	0·59	0·1 3 min.	0·3, 0·66, 0·53	Kitten. L. sciatic. 3 h. *post-mortem*. Temp. = 30°. Primary diminution and secondary augmentation.
A^l 406	0·39	0·29 to 0·15 4 min.	0·16 to 0·61	Rabbit. R. sciatic. 3 h. 45 m. *post-mortem*. Temp. 22° C. As 202. Marked secondary augmentation. *FIG.* 4.
A^j 405	0·70	0·56 to 0·3 5 min.	0·35 to 0·97	Rabbit. L. sciatic. 1 h. 10 m. *post-mortem*. As 406.
B^m 418	0·32	0·3, 0·42, 0·23 6 min.	0·64 to 0·33	Pigeon. L. sciatic. 3 h. *post-mortem*. Temp. = 37° C.

Tetanisation.

A^q 409	2·5	Tet. 5 min.	2·4	Rabbit. Branch of R. ant. crural. Temp. = 27°·5. 1 h. *post-mortem*.
A^r 410	2·3	Tet. 6 min.	1·8	Rabbit. Do., do. L. Temp. = 21°·5.
A^n 407	0·90	Tet. 5 min.	0·85 to 0·96	Rabbit. L. sciatic. Temp. = 20°.
A^t 411	0·86	Tet. 5 min.	0·92	Rabbit. R. sciatic. Temp. = 27°. *FIG.* 5. *Note.*—0·0005 volt compens. sent in after Tet. 2 h. 30 m. *post-mortem*.
C^{cc} 423	0·26	Tet 6 min.	0·26 to 0·19	Kitten. L. ulnar. Temp. = 36°·5 C. 3 h. *post-mortem*.

The values are taken from photographs. The action of these drugs on the nerves of warm-blooded animals is very similar to their effect on the nerves of the frog. Chloroform, ether, and carbon dioxide all produce diminution of the negative variation, followed by recovery in the case of the latter, with recovery or not in the case of $CHCl_3$, and the details of the process are clearly to be seen in figs.

The only difference that may be detected is that while in the frog the negative variation is increased by "little" $CHCl_3$ or Et_2O, and the abolition by "much" $CHCl_3$ and Et_2O is commonly followed by recovery to or beyond the normal; this increase has only been

observed in the bird (Experiment B') and not in the mammal. In the case of CO_2 this increase is seen in all the warm-blooded nerves; primary and secondary augmentation are shown in Exp. B^m from the pigeon, and the latter, in fig. 4, from the rabbit.

I do not here enter upon any discussion of the actual mechanism of this increase, it may be due to either of two causes—increase of E.M.F. or increased duration of electromotive change. The latter explanation has been suggested by Gotch as being the true one.

The effect of tetanisation (fig. 5) has not been marked. Three experiments proved negative, and two gave a slight increase, so that this question is still undecided.

It appears, therefore, certain that neither in the voltage of the negative variation, in the strength of excitation, or in the action of anæsthetics is there any marked difference between the warm-blooded and amphibian nerves, and that all the facts ascertained for the latter under these heads can be applied *en bloc* to the former.

Temperature of Extinction by Heat.

Three series of experiments on frogs, mammals, and birds were undertaken to ascertain the precise point at which the negative variation was abolished by heat.

Method.—The nerve chamber was kept at a constant temperature throughout, *e.g.*, 30° C. The nerve itself was placed on the electrodes, and when it had reached the temperature of the chamber, the value of 0·001 volt was determined on the galvanometer scale, and then the values of the first six negative variations. The nerve was then removed, placed in 1·05 per cent. NaCl solution (containing Ca salts, &c.) at the desired high temperature (*e.g.*, 49° C.), left for exactly 5 minutes, placed in cool (18° C.) salt solution for 7 minutes. A fresh transverse section was made, the nerve was replaced on the electrodes, and the value of 0·001 volt and the second set of six negative variations determined.

This method fulfils several *desiderata*.

(1.) It is possible to keep the beaker of hot saline solution at any given temperature with an error of less than $\pm$ 0·1° C.

A standardised thermometer was placed in the bath close to the nerve, and with 5 minutes immersion all parts of the nerve reach the temperature of the solution.

(2.) Any alteration in the resistance of the nerve is readily detected by means of the standard deflection with 0·001 volt, and as both readings are taken at the same temperature, this alteration must be a permanent one, and not the temporary alteration always seen when a nerve is heated or cooled.

(3.) Using a concentration of salt solution* that had been found to

* No carbohydrate was added to the solution in any of the heat experiments. The solution was neutral.

work equally well with all classes of nerve, and carefully preserving similar conditions of experiment, the results in the different series are strictly comparable not only with each other, but also with Halliburton's* researches on the heat-coagulation of the nerve proteids.

The excitation was a maximal one throughout.

Series I.

A. With Laboratory Frogs.
B. With freshly-caught vigorous Frogs.
Sciatic nerve. Excitation 30, except in A^e.

Experiment No.	Hours *post-mortem*.	Temp. of nerve chamber.	Temp. of hot bath.	Neg. var. initial $= a$. 0·001 v.	Neg. var. final $= b$.	Irritability quotient $= \frac{b}{a}$.	Notes.
	h. m.						
A^e	1 0	room	43°·5	1·0	0	0	A.
A^f	2 7	,,	40·7	0·8	0	0	
A^{ha}	5 0	,,	40·0	1·2	0	0	
A^{hb}	5 30	,,	39·0	1·8	0·56	0·31	
A^g	2 30	,,	38·5	1·7	1·7	1·0	
A^z	6 0	17° C.	42·1	2·5	0	0	B.
A^w	2 40	,,	42·0	2·3	0	0	
A^y	3 30	,,	41·1	1·8	0·91	0·51	
A^v	2 0	15° C.	40·0	·7	3·0	1·7	

Series II.

Rabbit. Sciatic. Excitation 1000 for first three experiments, last four, 500.

Experiment No.	Hours *post-mortem*.	Temp. of nerve chamber.	Temp. of hot bath.	Neg. var. initial $= a$. 0·001 v.	Neg. var. final $= b$.	Irritability quotient $= \frac{b}{a}$.	Notes.
	h. m.						
B^{fa}	6 30	33°·0	48°·5	0·53	0·12?	0·22?	Doubtful return.
B^{ca}	3 30	29·0	48·0	0·57	0	0	
B^d	5 30	30·0	47·7	0·83	0·25	0·30	
A^n	4 0	20·5	46·0	1·1	0·45	0·41	
A^p	6 35	21·0	44·3	0·52	0·34	0·65	
A^m	5 0	19·0	42·3	0·48	0·52	1·1	
A^k	2 45	19·0	39·5	0·76	0·69	0·91	

* Halliburton. "Croonian Lecture," 1891, and below.

Series III.

Pigeon. Experiments B^u and B^s Sciatic, all the rest Median.

Experiment No.	Hours *post-mortem*.	Temp. of nerve chamber.	Temp. of hot bath.	Neg. var. initial $= a$. 0·001 v.	Neg. var. final $= b$.	Irritability quotient $= \frac{b}{a}$.	Notes.
	h. m.	°	°				
C^{fb}	3 15	28	53·6	0·30	0	0	Cold bath accidentally omitted. The nerve was much contracted longitudinally after heating.
C^{fc}	4 0	30	53·0	0·75	0	0	Nerve contracted. No "negative variation" after heating, but large positive current escape observed, not abolished by crushing.
B^u	4 15	38	52·5	0·25	0·12	0·48	Neg. var. rapidly diminishing.
B^k	4 30	38	52·0	0·56	0·17	0·30	
B^j	3 0	37	50·0	0·61	0·18	0·30	
B^g	2 0	30	45·3	0·30	1·05	3·5	

The experiments can be summarised thus :—

	Normal temp. of animal.	Temp. of incr. neg. var.	Temp of dim. neg. var.	Temp. of abolished neg. var.
Frog	—	39—40° C.	39—41°	40—42°
Rabbit.....	37—41°*	42·3°	44·3—47·7°	48—49°
Pigeon.....	40—42·5†	45·3°	50°	52—53°

It is seen that the effect of heat occurs in three stages. In the first, at a temperature of 1—2° above that of the animal, the negative variation is increased. In the second there is diminution, recovered from at the lower temperatures (4° over normal) if the nerve is cooled longer than the standard time, not recovered from at the higher (6—7° over normal), and finally the negative variation is permanently abolished, 8° over normal in the rabbit, 10° in the pigeon.

While the mammalian and avian nerves show quite small individual

* Pembrey (Schäfer's 'Text-book,' vol. 1, p. 790). The higher limit for the rabbit is from unpublished observations of Dr. Pembrey, which he has very kindly furnished me for this paper.

† Corin and Van Beneden, 'Arch. de Biol.,' Gand., 1887, vol. 7, p. 265.

differences in different animals as regards their reaction to heat, the frog's nerve varies a little according to the condition of the animal, and so the observations have been arranged in two divisions. Here one also notices that the "injury range" is very much smaller than in the warm-blooded nerve, 2° at most separating a temperature that has no ill effect for one that finally kills the nerve, as against 5—6° in the mammal and bird.

Observations.

A summary of the previous work on the effect of temperature on nerves is to be found in Howell's* paper, and in that of Boycott (*loc. cit.*).

Howell, from his own researches, gives 41—44° as the temperature at which conductivity is abolished in frog's nerve, the other authors give 45—50°. The difference appears to be due to the methods employed. Hitherto, there has been some difficulty in ensuring that all parts of the nerve shall have the same temperature, and this temperature has in most cases been ascertained indirectly, further, the time during which the temperature is kept up and the conditions of moisture, &c., greatly influence the results.†

Another explanation is possible. The majority of observers‡ have examined the conductivity of nerve as opposed to the excitability, and if the two processes are supposed to be distinct, it might be said that the excitability was extinguished before the conductivity. In view of the considerations stated above, and also of the relation to the coagulation point of the proteids, this hypothesis does not seem to be well founded.

The relationship of the extinction point given above and the coagulation point of the proteids in the body of the animal is a very close one. In the frog, the first coagulation of extracted muscle proteid occurs at 40° C,§|| the first step in heat rigor of the muscle itself at 38—40°,¶ the electrotonic currents are abolished at 40°,** and the extinction point of the nerves as determined above, 40—42° C.

In the rabbit the proteid coagulation occurs at 47°,§|| the muscle

* Howell, Budgett and Leonard, "J. Physiol.," vol. 16, p. 298.

† Some earlier experiments I have made under different conditions lend support to these remarks.

‡ Except Edwards' 'J. Hopkins Lab. Studies,' vol. 4, 1887, p. 18 (45—48° —55°?); and Moriggia, 'Moleschott's Untersuchungen,' vol. 14, p. 382 (46—47°).

§ Halliburton, *loc. cit.*; also Halliburton and Mott, 'Archives of Neurology,' vol. 2.

|| Von Fürth, 'Arch. f. Exper. Path. u. Pharmak.' Leipzig, 1895, vol. 36, p. 231, and *ibid.*, vol. 37, 1896, p. 389.

¶ Vincent and Lewis, 'J. Physiol.,' vol. 36, p. 445; see also Brodie and Richardson, 'J. Physiol.,' vol. 21, 1897, p. 353, and 'Phil. Trans.,' B, vol. 191, 1899, p. 127; and also Vernon, 'J. Physiol.,' vol. 24, p. 239.

** Waller, 'Roy. Soc. Proc.,' vol. 60, p. 384.

rigor at 45—50°C,* and the nerves die at 48—49°. The proteids of the cat's brain coagulate at 47° C.† No data for the bird are available,‡ the nerves die at 53°.

In table form.

	Frog.	Mammal.	Bird.
Muscle proteid (Halliburton and von Fürth)	40°	47°	—
Muscle rigor (Vincent and Lewis)	38—40°	45—48°	—
Nerve proteid (Halliburton)	—	47°	—
Nerve electrotonic currents (Waller)	40°	—	—
Nerve (present experiments)	40—42°	48—49°	53°

It is reasonable to conclude from these figures that the extinction of the irritability of the nerve is due to the coagulation of the proteids which enter into its composition, and I venture to forecast, that when the proteids of the frog's nervous system are examined one will be found to coagulate at 40°, and that the two proteids coagulating at 40° and 47° are absent from the nerves of the bird. It is possible, therefore, to make a nearer approach to the analysis of actually living nerve substance than has been practicable hitherto.

Temperature of Extinction by Cold.

Method.—Alongside the nerve in the nerve-chamber, was placed a junction (A) of konstantan and iron wire, and the nerve was arranged so as to touch this. The junctions konstantan copper (B) and iron-copper (C) were placed in glass tubes and immersed in water at room-temperature, the two copper terminals led to a key-board, with connections to a sensitive Kelvin-type galvanometer of low resistance (16 ohms), and a compensating circuit arranged as shown. The wire rheochord marked 1 ohm was of the ordinary du Bois-Reymond type, and with the voltage and added resistance as marked 1° difference between the junction A, and B C, was represented by about thirty-five scale divisions. The compensating current was furnished from an accumulator of large capacity. It was found after careful tests that no perceptible alteration (within 0·05°) of the

* Vincent and Lewis, 'J. Physiol.,' vol. 36, p. 445; see also Brodie and Richardson, 'J. Physiol.,' vol. 21, 1897, p. 333, and 'Phil. Trans.,' B, vol. 191, 1899, p. 127; and also Vernon, 'J. Physiol.,' vol. 24, p. 239.

† Halliburton, *loc. cit.*; also Halliburton and Mott, 'Archives of Neurology," vol. 2.

‡ Demant, 'Zeitschr. f. Physiol. Chemie,' vol. 3, p. 241, and Kühne and Chittenden, 'Zeitschr. f. Biol.,' N. F., vol. 7, p. 358, 1889, have made some observations on this point, but I have been unable to consult the papers.

temperature of the fixed junction took place, if it did, a correction could be readily applied to the figures obtained. To guard against current escape from one circuit to another all the wires leading to the nerve chamber were placed within rubber tubing, and the konstantan-iron junction (A) was coated with rubber "tyre-repairing" solution, which on drying left a thin and even coat of rubber on the surface, insulating it from any nerve currents and from any possible mutual action from or to the nerve. It was found by experiment that no such action occurred.

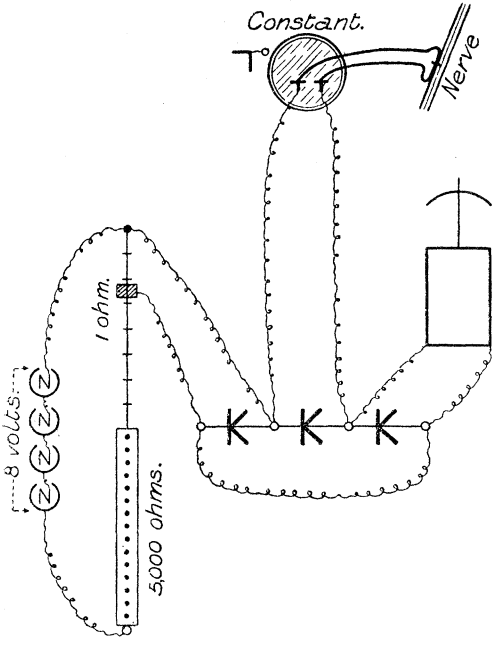

FIG. 6.

To graduate the instrument the junction A was placed in melting ice, the thermo-current compensated till the galvanometer spot stood at zero, and the compensator scale read off. This was repeated with hot water when it was desired to use a temperature higher than the constant of B C. This graduation was performed as a matter of precaution at the commencement of each day's experiments. The whole apparatus proved simple and convenient to use, and of an accuracy much in excess of what proved necessary in these experiments. And as the junction A actually touches the nerve, there can be no doubt that the actual temperature of the latter is observed. The readings are given to 0·1°C. The nerve chamber was cooled by being placed in a tin box, outside which was a layer of ice and salt,

Experiments.

Abstract.

Animal.	Experiment No.	Initial neg. var. 0·001 volt.	Nerve.	Extinction point.	Limits.	Notes.
Frog	B^{p}	2·0 q.p.	Sciatic	−3°·5 C.	−3°·5 C.	
Hedgehog*.....	C^{da}	0·12	Ext. popliteal	+6°·4	+ 6·4 to −1° 4	C^{dc} was a 2nd experiment with the same nerve as C^{dc}.
,, ...	C^{dc}	0·40	Int. popliteal	+2°·6		
,, ...	C^{df}	0·44	,,	−1°·3		
,, ...	C^{dc}	0·32	,,	−1°·4		
Rabbit.....	B^{ab}	0·89	Int. popliteal	+7°·4	+7°·4 to +3°·8	
,, ...	C^{dc}	0·54	Ext. popliteal	+7°·1		
,, ...	C^{db}	0·60	Int. popliteal	+3°·8		
Pigeon.....	C^{ea}	0·45	Median	+8°·2	+8°·2 to +6°·9	
,, ...	C^{eb}	0·75	Median	+6°·9		

* Dr. Pembrey very kindly furnished me with these animals in a state of hibernation.

using the same apparatus that Waller* employed in his researches of the effect of temperature on the electrotonic current of frog's nerve.

The negative variation was observed in the way before mentioned. The value of the galvanometer deflection was ascertained by taking the scale value of 1 millivolt at intervals. It was found, as is well known, that the resistance of the nerve and electrodes gradually increased as the temperature was lowered, and this causes a small error in the strength of excitation, though this was annulled as far as possible by an added resistance of 100,000 ohms in the exciting circuit.

Comments.

The limits determined are for the temporary abolition of the negative variation, not for its permanent abolition. There is a gradual rise of the extinction point through the four classes of amphibians, hibernating mammals, mammals and birds. The limit varies a little in each experiment in a manner that is not accounted for by either the apparent condition of the nerve or by its anatomical character. That some variation was to be expected was clear from the researches of Howell,† who found that the vaso-constrictor fibres in the cat's sciatic were paralysed by cold (+4° C. *q.p.*), while the vaso-dilatator fibres were paralysed 1° lower, and even greater differences were observed between the cardiac and respiratory fibres in the vagus.

Taking the experiments as they stand, it is evident that those upon which most reliance can be placed, are where the nerve has reached

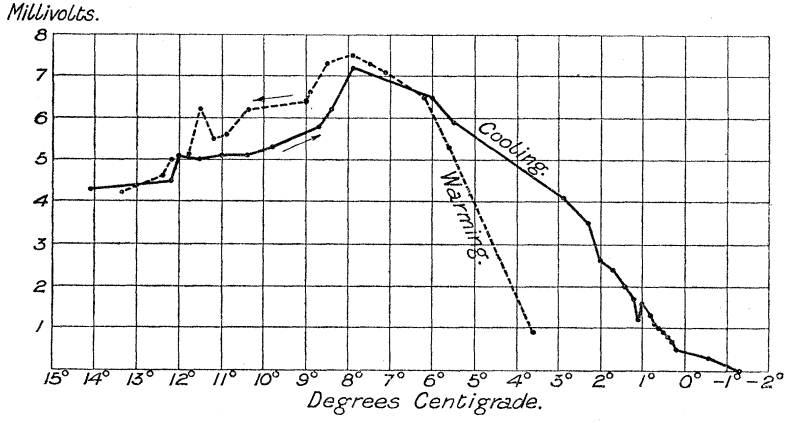

FIG. 7.—Exp. C[af]. Value of the negative variation in nerve of hedgehog at different temperatures.

* Waller, 'Proc. Physiol. Soc.' in 'J. Physiol.,' vol. 20.

† Howell, *loc. cit.*

the *lowest* point before extinction of the negative variation took place, and both the frog and hedgehog agree in giving a measurable response below 0°. In experiment B on the frog the negative variation reached a maximum at +3°·8 C. In the experiment C^{df} on the hedgehog an exactly similar maximum was observed at +7°·9 C., and plotting out the "cooling" and "warming" curves the latter gave also a maximum at the same point (fig. 7).

No such maximum was certainly observed in the mammal or pigeon. There were traces of a maximum at 25° C. in the former (in experiment B^{ub} and an earlier experiment on the kitten not recorded above), but the experiments C^{dg}, C^{dh}, C^{ed}, C^{eh} showed no sign of this. Several explanations are possible, but it seems preferable to await the result of further experiments before insisting too strongly on any of them. One, however, seems well established, that the negative variation follows the temperature with a certain "lag." This is seen to a small extent in the nerve of the hedgehog (fig. 7), in the rabbit and bird it is larger in amount, and tends to obscure curves taken in this way.

I have not yet determined the *permanent* extinction point, recovery took place in experiment B^{p} in the frog after a temperature of −3°·5 C. had been reached, and in Experiment B^{ub} on the rabbit (−2°·5), experiments are in progress in this direction.

The range of temperature through which the nerve can function is obtained by combining the figures here observed with those of the former series, and it is found that this range is the same for all the nerves examined, 45°·5 for the frog, 45°·2 for the rabbit, and 46°·1 for the pigeon, one step higher in the temperature scale in each case (Fig. 8).

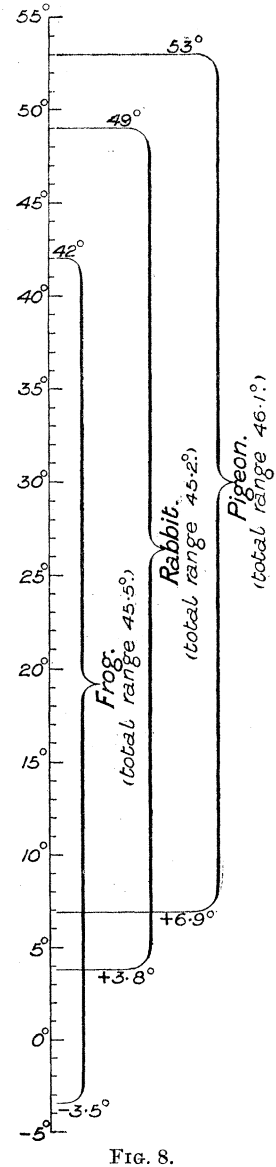

FIG. 8.

Conclusion.

(1.) It is possible to examine isolated mammalian and avian nerves under the same conditions as frog's nerves.

(2.) There is no essential difference between the nerves of frogs, mammals, and birds as regards their negative variation, excitability, and reaction to anæsthetics.

(3.) There is a marked difference in the extinction point for heat. The negative variation in frog's nerve is abolished at 40—42° C., in rabbit's nerve at 48—49°, in pigeon's nerve at 53°.

(4.) This extinction point corresponds closely with the first coagulation point of the body proteids, where these are known, and thus coagulation is probably the cause of the permanent loss of irritability of the nerve.

(5.) The point at which the nerves are paralysed by cold is $-3°{\cdot}5$ in the frog, $-1°{\cdot}4$ in the hedgehog, $+3°{\cdot}8$ in the rabbit, and $+6°{\cdot}9$ in the pigeon.

It gives me great pleasure to acknowledge my indebtedness to Dr. A. D. Waller for his great kindness and assistance in everything connected with this paper.

"On the Decline of the Injury Current in Mammalian Nerve, and its Modification by Changes of Temperature. Preliminary Note." By S. C. M. Sowton and J. S. Macdonald. (From the Thompson-Yates Laboratory of Physiology, University College, Liverpool.) Communicated by Professor C. S. Sherrington, F.R.S. Received December 10, 1902,—Read February 12, 1903.

The sciatic nerve of a freshly-killed frog led off from transverse section and longitudinal surface to a galvanometer, gives a current of injury which, as Engelmann* and others have pointed out, is greatest immediately after the section has been made. If tested at frequent intervals, it is found that from the outset the E.M.F. rapidly diminishes. A continuous record of the decline of the current may be obtained, by photographing the movement of the galvanometer spot, using for the purpose the method devised by Dr. Waller, and fully described in his papers.† The nerve with its electrodes being inclosed in a moist chamber, such an observation may be prolonged almost indefinitely. The curve is convex to its abscissa, the decline being rapid at first and gradually diminishing in speed.

If the injury current of fresh mammalian nerve be examined in a similar way, the records show in many cases a marked difference of curve, the decline being often very gradual; some records even

* Engelmann, 'Pflüger's Archiv,' vol. 15, pp. 116—148.

† S. C. M. Sowton, 'International Congress,' Cambridge, 1898.